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Assessment of changes in the expression profile of selected genes encoding epigenetic enzymes in blood cells as potential diagnostic and/or prognostic ᴿbiomarkers of gastric cancer

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Introduction

Gastric cancer is one of the leading malignancies, ranking fifth in frequency of diagnosis and fourth cause of death from cancer worldwide. Each year, there is more than one milion new cases of gastric cancer. Although there is a decreasing trend in the global gastric cancer incidence rates, recent findings indicate an increasing trend of non-cardia gastric cancer among non–Hispanic whites aged <50 years. Gastric cancer is usually diagnosed at an advanced stage, so the mortality rates remain high. The poor prognosis is reflected in the 5-year survival rate, which in Poland is less than 25%. For the advanced stage of gastric cancer, median survival is less than 12 months. In patients with non-cardia adenocarcinoma, who were treated surgically, the 5-year survival rate decreases from 59% for stage 0-I tumors, to 18% for stage III-IV tumors. That underlines the importance of early gastric cancer detection.

RNA methylation in gastric cancer

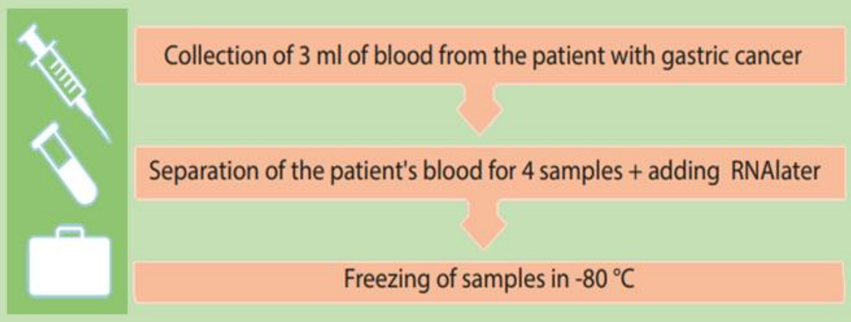
Recently, many studies have been paying attention to n6-methyladenosine (m6A) RNA modification. Dysregulation of m6A RNA methylation may be involved in the initiation and progression of many malignancies. Scientists suspect that m6A RNA methylation is also involved in carcinogenesis and progression of gastric cancer.

Therefore we examined the expression of the following genes: METTL3, METTL14, METTL16, FTO, ALKBH5, WTAP which ale involved in the regulation of RNA methylation.

Materials & Methods

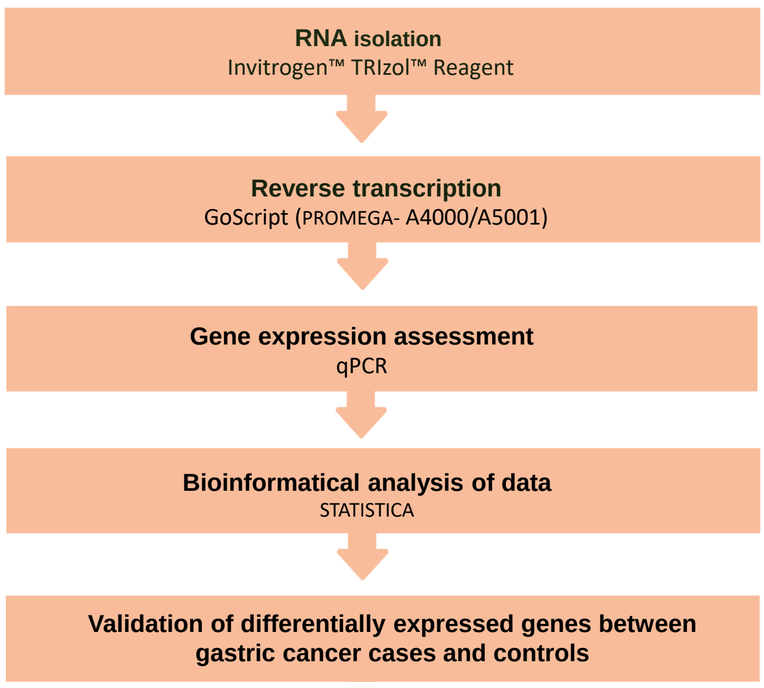
Samples collection

1. The in vivo model includes human peripheral blood samples from the group of gastric cancer patients and from matched (gender, age, and ethnicity) healthy individuals as a novel approach of liquid biopsy.
2. The material for molecular tests are blood samples (3 ml) taken for K2EDTA, single-use tubes, from patients during diagnostic tests before surgery and from volunteers not suffering from malignant tumors.
3. Blood samples are stored at -80 °C and then used for molecular testing.



The collection of the samples took place in the Department of Oncological Surgery, Department of Oncology, Medical University of Lodz.

Molecular testing and analysis



METTL16- Methyltransferase 16

METTL16 is one of the genes encoding enzymes that play role as writers– methyltransferases with the ability to catalyze m6a formation.

Figure 1
Expression of METTL16 in control and gastric cancer group (samples 1-10)

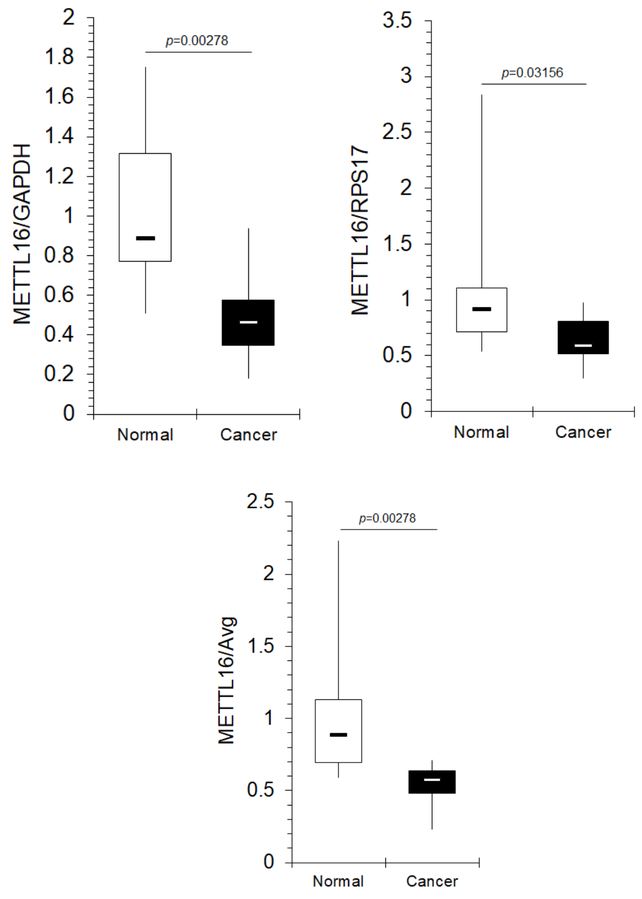
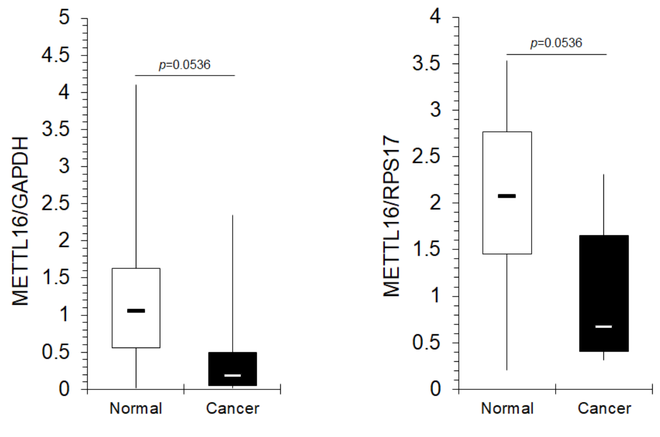
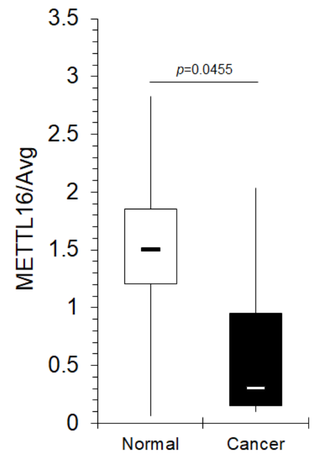


Figure 2
Expression of METTL16 in control and gastric cancer group (samples 11-20)



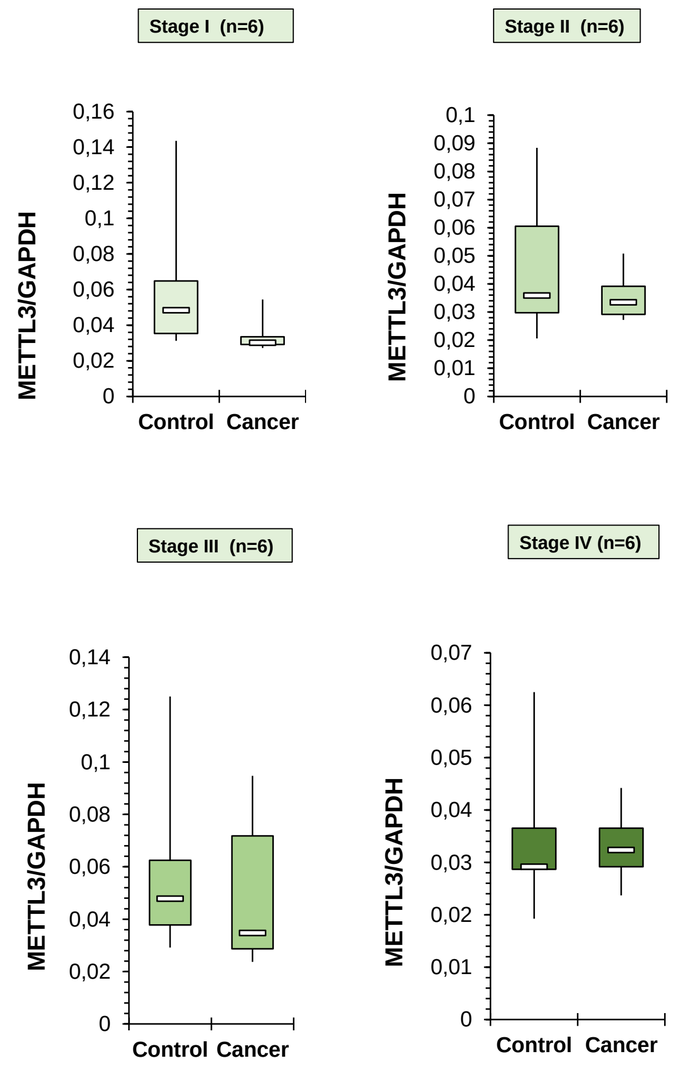
Expression of METTL16 in control and gastric cancer group (samples 11-20)



METTL3 –Methyltransferase 3

METTL3 is one of the genes encoding enzyme involved in the regulation of RNA methylation. Data suggest dysregulated expression of METTL3 in cancer.

Figure 3
Expression of METTL3 – gastric cancer stages



Conclusions

- The blood samples, an easily accessible biological material, as well as a simple and fast test of gene expression (qPCR) analysis, used as an effective diagnostic tool, seem really promising and easily implemented in the clinic.
- Preliminary analysis suggests a decrease in METTL16 expression among gastric cancer patients, and a decrease in METTL3 expression, especially in the first stages of cancer advancement.
- Possible candidates for molecular diagnostic and prognostic biomarkers of gastric cancer will be subjected to a patent application.

The decision of the Bioethics Committee of the Medical University of Lodz, received on May 11, 2021, No. RNN/133/21/KE